in vitro use of the hybridomas for priming autologous T cells before reinfusion of the T cells for an antitumor response. Applicants contend that the reference would not enable one skilled in the art to practice the claimed invention, and would not have given one skilled in the art a "reasonable expectation of success" that the present invention could be practiced.

Page 16 of the reference states:

> For the induction of an anti-tumor immune response in vitro, the DLC/tumor cell hybridomas are irradiated or otherwise inactivated, and cultured with the immune cells of the patient. The activated immune cells are then re-injected into the patient.

This is the only "teaching" in the entire specification, including the examples, of the use of "hybridoma cells for priming autologous T cells before reinfusion of the T cells for an antitumor response . . . ." Applicants respectfully submit that this is not an enabling teaching. The reference fails to teach culture conditions or parameters, the types of immune cells that would be appropriate, methods for harvesting the immune cells from the co-culture, or the manner in which injection of the allegedly activated immune cells should be effected, such as the effective doses, frequency of doses, and the like. Significantly, there is no evidence whatsoever in the reference that such a method would be effective. Indeed, page 32 of the reference indicates that the hybridomas failed to express constitutively T-cell activating molecules, and had to be stimulated with cytokines to induce such expression. Thus, one skilled in the art could not read the reference and know how to practice the present invention, and more importantly, would not have a reasonable expectation that the present invention would work based upon the teachings of the reference.

A reference must be enabling if it is to be regarded as prior art, just as a patent application must be enabled. (See, for example, *W.V. Akzo v. International Trade Commission*, 808 F.2d 1471, 1 USPQ2d 1241, 1245 (Fed. Cir. 1986); and *In re Brown*, 141 USPQ 245 (CCPA 1964), copies of which are enclosed). All that appears in the reference is speculation that the hybridomas can be used to activate immune cells, and that the activated immune cells will then elicit an anti-tumor response in a patient, with no teaching of the means by which the

present methods could be practiced, nor any teaching that such methods would even be successful. There is no direction or guidance presented whatsoever of the present methods in the references. Thus, it is submitted that the reference does not enable the claimed invention.

In addition, a reference cited under Section 102 must contain sufficient technical information to enable a person skilled in the art to make and use the claimed invention without undue experimentation or unobvious contributions. (See, for example, *In re Hoeksema*, 399 F.2d 269, 158 USPQ 596 (CCPA 1968); *In re LeGrice*, 301 F.2d 929, 133 USPQ 365 (CCPA 1962), copies of which are enclosed). One skilled in the art simply could not, upon reading the reference, generate antigen specific T cells in the manner taught in the present invention. Accordingly, Applicants respectfully submit that Moser is not a proper reference and that the claims are allowable over the art.

Applicants further respectfully submit that the reference is not appropriately cited under 35 U.S.C. § 102 against Claims 8-12. For a reference to be properly applied under Section 102, the reference must show every facet of the claimed invention. The reference does not show every element of Claims 8-12.

Claim 8 recites that the hybridoma contains a ratio of first cells to second cells of about 6:1. The reference does not teach a ratio of dendritic cells to tumor cells greater than 2:1. The Office Action states that the ratio is not seen as critical in the ability of the hybridoma to stimulate T cells. As noted in the specification, however, the ratio of 6:1 is preferred in the present methods to yield a sufficient number of DC/tumor cell hybridomas, which are then used in co-culture with T-cells. While lower DC and tumor cell ratios are within the current invention, they may not yield sufficient numbers of hybridomas for use in the present methods. (See Specification, page 7, lines 8-13.)

Claims 9-11 are directed to methods wherein the first cell and second cell are co-cultured. The reference is silent as to use of any dendritic cell/tumor cell preparations other than hybrids or hybridomas. Page 13 of the reference states that, "After fusion, the treated cells include a plurality of DLC/tumor cell hybrids, as

well as unfused tumor cells and unfused DLCs" (emphasis added), but there is no specific teaching that dendritic cells and tumor cells be co-cultured instead of fused. In contrast, Claims 9-11 recite that the first and second cells are co-cultured; as described in the specification, including the examples, a co-culture methodology is used wherein no fusion aid (i.e, PEG) is added. The reference fails to teach the co-culture as recited in Claims 9-11.

Claim 12 recites that the T cells are added in a ratio of 10:1 and 100:1 of T cells to dendritic cells. As noted above, the reference is completely silent as to how to stimulate T cells using hybridomas. Accordingly, the reference cannot teach the ratio recited in Claim 12.

For all of the above reasons, Applicants respectfully submit that the present claims are patentable over the art of reference. The reference is not enabling for the present methods, and is further silent as to the use of a dendritic cell to tumor cell ratio of 6:1, co-culturing dendritic cells and tumor cells, and a ratio of T cells to dendritic cells of between 10:1 and 100:1.

SUMMARY

For all of the above reasons, Applicants respectfully submit that the present claims are in condition for a Notice of Allowance. Such action is respectfully requested at an early date.

Respectfully submitted,

Diane R. Meyers
Registration No. 38,968
Eckert Seamans Cherin & Mellott, LLC
600 Grant Street, 44th Floor
Pittsburgh, PA 15219
Attorney for Applicants

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(412) 566-2036